

Claims

1. An epitope for binding integrins, comprising strands A and G of domain 1 of ICAM-4 (SEQ ID NO: 1), in which the A strand (SEQ ID NO: 2) is defined by amino acid residues 17 to 27 of ICAM-4 and the G strand (SEQ ID NO: 3) is defined by amino acid residues 90 to 100 of ICAM-4, or a functional homologue of the epitope.
2. The epitope according to claim 1, defined by amino acid residues F18, W19, V20 on the A strand of ICAM-4 and amino acid residues R92, A94, T95, S96 and R97 on the G strand of ICAM-4.
3. The epitope according to either of claim 1 or claim 2, modified in that the A strand is replaced by strand F on domain 1 of ICAM-4, in which the F strand (SEQ ID NO: 4) is defined by amino acid residues 77 to 87 of ICAM-4.
4. The epitope according to claim 3, defined by amino acid residues W77 and L80 on the F strand of ICAM-4 and amino acid residues R92, A94, T95, S96 and R97 on the G strand of ICAM-4.
5. The epitope according to any preceding claim, further defined by amino acid residues W66 on the E strand of domain 1 of ICAM-4 and K118 on the B strand of domain 2 of ICAM-4, in which the E strand (SEQ ID NO: 5) is defined by amino acid residues 160 to 170 of ICAM-4 and the B strand (SEQ ID NO: 6) is defined by amino acid residues 116 to 126 of ICAM-4.
6. The epitope according to any preceding claim, further defined by amino acid residues N160, V161 and T162 on the E strand of ICAM-4.
7. The epitope according to any preceding claim, in which the integrins are α_v integrins (for example, as found on HT1080 cells), $\alpha_4\beta_1$ (also known as VLA-4; for example, as found on HEL cells and erythroblasts), or $\alpha_5\beta_1$ (for example, as found on erythroblasts).

8. A footprint domain for binding integrins, comprising a first epitope as defined in any of claims 1 to 6 and a second epitope comprising the C and F strands of domain 1 of ICAM-4 and the CE loop of domain 2 of ICAM-4, in which the C strand (SEQ ID NO: 7) is defined by amino acid residues 47 to 54 of ICAM-4, the F strand (SEQ ID NO: 4) is defined by amino acid residues 77 to 87 of ICAM-4 and the CE loop (SEQ ID NO: 8) is defined by amino acid residues 150 to 158 of ICAM-4, or a functional homologue of the footprint domain.
9. The footprint domain according to claim 8, in which the second epitope is defined by amino acid residues R52 on the C strand of ICAM-4, W77 and L80 on the F strand of ICAM-4, T91, W93 and R97 on the G strand of ICAM-4, and E151 and T154 on the C'-E loop of ICAM-4.
10. The footprint domain according to either of claim 8 or claim 9, in which the integrin ligands are α_v integrins (for example, as found on HT1080 cells), VLA-4 (for example, as found on HEL cells) and/or the β_2 -family of integrins (such as Mac-1, for example, as found on leucocytes and on neutrophils, and/or LFA-1), including $\alpha L\beta 2$ (for example, as found on neutrophils).
11. An antagonist of the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10.
12. An antagonist of a ligand for the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10.
13. The antagonist of claim 12, having or consisting essentially of three, four, five, six, seven, eight, nine or more amino acid residues of the A, C, F or G strands or the CE loop of ICAM-4, or a functional homologue thereof.
14. The antagonist of claim 14, in which the antagonist has or consists essentially of the amino acid sequence according to SEQ ID NO: 9, SEQ ID NO: 10 or SEQ ID NO: 11.

15. A method of antagonising the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10, comprising the step of contacting the epitope and/or the footprint domain with the antagonist of claim 11.
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16. A method of antagonising a ligand of the epitope of claims 1 to 7 and/or the footprint domain of claims 8 to 10, comprising the step of contacting the ligand with the antagonist of any of claims 12 to 14.
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17. Use of the antagonist of any of claims 11 to 14 for treating a disease.
18. The use according to claim 17, in which the disease involves ICAM-4.
19. Use of the antagonist according to any of claims 11 to 14 in the manufacture of a
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- medicament for the treatment of a disease involving ICAM-4.
20. The use according to any of claims 17 to 19, in which disease is characterised by increased levels of ICAM-4 binding.
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21. The use according to any of claims 17 to 19, in which the disease is characterised by decreased levels of ICAM-4 binding.
22. The use according to any of claims 17 to 21, in which the disease is sickle cell disease, deep vein thrombosis (DVT), malaria, heart disease, vascular complications,
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- diabetes, β -thalassemia or a thrombotic complication of haematological diseases.
23. An isolated nucleotide encoding the epitope defined in claims 1 to 7 or the footprint domain of claims 8 to 10 or the antagonist of claims 11 to 14.
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24. The isolated nucleotide of claim 23, having a sequence defined within the sequence of SEQ ID NO: 12.